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## Decoupling of omicron variant infections and severe COVID-19

SARS-CoV-2 omicron (B.1.1.529) was designated a variant of concern by WHO because of specific mutations that might increase transmissibility, risk of reinfection, or vaccine breakthrough infection. Many of these mutations affect the receptor-binding domain and N-terminal domain of the spike protein, which might, paradoxically, increase binding to ACE-2 while evading antibody recognition.<sup>1</sup>

Emergence of omicron appears to have parallels with the beta variant (B.1.351) in South Africa. It was demonstrated that there are decreased neutralising antibody titres with beta in infection-naïve individuals who received two doses of AZD1222 (ChAdOx1 nCoV-19) or BNT162b.<sup>2,3</sup> Nevertheless, real-world data showed more than 80% effectiveness against severe disease and hospitalisations.<sup>4,5</sup>

Although preliminary evidence suggests booster doses might enhance protection against omicron,<sup>6</sup> studies are underway to fully determine vaccine effectiveness. Given the natural lag between infection and severe outcomes, we await further data on omicron for effectiveness of vaccinations in preventing severe disease—the key intended outcome of vaccination.<sup>7</sup> In the meantime, the South Africa National Institute for Communicable Diseases has shared preliminary data indicating a decoupling of infection rates from hospitalisations and deaths with omicron. These data suggest underlying immune responses following infection and that primary and booster vaccination might attenuate the course of illness.

Complementary humoral (antibody) and cellular (T cell) immune responses are activated following natural SARS-CoV-2 infection or vaccination. T-cell responses encompass a broad range of spike-protein-specific T-cell receptors that recognise

multiple epitopes both within and outside of mutated regions in variants of concern.<sup>8</sup> Thus, even if spike protein mutations enable neutralising antibody escape, non-neutralising antibodies or T-cell-mediated responses can provide protection. The beta variant has only a few mutations in the spike gene that affect T-cell epitopes, meaning T-cell response is maintained; this is expected to be the case with omicron.<sup>1,8</sup>

At this stage of the pandemic, omicron is spreading in populations where many individuals have been previously infected with SARS-CoV-2 and are now being vaccinated, or where many have received two or three COVID-19 vaccine doses. These populations might be expected to have greater depth of antibody response and a broader and deeper poly-epitopic T-cell response,<sup>9,10</sup> which should overcome some of the anticipated antibody evasion of omicron. In these scenarios, protection against severe disease is anticipated. Most cases of severe disease and hospitalisation with omicron are among the unvaccinated; we recommend an accelerated and equitable roll-out of COVID-19 vaccines, which have a continued role in enhancing protection against omicron.

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[https://www.who.int/news/item/26-11-2021-classification-of-omicron-\(b.1.1.529\)-sars-cov-2-variant-of-concern](https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern)

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